REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated November 1, 2007 are respectfully requested. This amendment is accompanied by a separate petition for a two-month extension of time to extend the date for response to April 1, 2008.

I. Amendments

Independent claims 1 and 19 are amended to recite that the polymeric film reduces or prevents the interaction of the second drug and the first drug prior to ingestion, which dissolves in the gastrointestinal fluid upon ingestion. Support for this amendment can be found, for example in paragraphs [0004], [0006], [0015], and [0017].

Paragraphs [0030]-[0031], corresponding to Example 2, have been amended to change the tense of verbs, indicating that Example 2 is prophetic.

II. Rejections under 35 U.S.C. § 103

Claims 1-28 were rejected under 35 U.S.C. § 103 as allegedly obvious in view of Johnson *et al.*, U.S. Patent No. 6,171,618 (herein "Johnson").

Claims 1-28 were rejected under 35 U.S.C. § 103 as allegedly obvious over Johnson in view of Timmins *et al.*, U.S. Patent No. 6,031,004 (herein "Timmins") and Sauerberg *et al.*, U.S. Patent No. 6,274,608 (herein "Sauerberg").

These rejections are traversed in view of the foregoing amendments and following remarks.

A. The Present Claims

Independent claim 1, as amended, is directed to a method for the manufacture of a pharmaceutical tablet. The method includes in step (b) "depositing on a surface of said unitary body *a polymeric film effective to reduce or prevents the interaction of the second drug and the first drug, which is dissolved in the gastrointestinal fluid upon ingestion.*

B. The Cited Art

Johnson relates to a dosage form comprising a core for delivering a first drug (pseudoephedrine) in a sustained release manner and an exterior coating for delivering a second drug in an immediate release manner (col. 2, line 66 – col. 3, line 27; col. 3, lines 28-45). The core may be surrounded by a permeable membrane with pores or holes (col. 3, lines 17-27; col. 5, lines 9-32 and 60-64; col. 7, line 49 – col. 11, line 5). The preferred material for the membranes are typically "insoluble film forming polymers and waxes," such as cellulose acetate, ethyl cellulose, and thermoplastics (col. 9, lines 2-9). The exemplified insoluble films are cellulose acetate and ethyl cellulose (col. 15, lines 9-28; col. 18, lines 1-13; col. 19, lines 1-11; and col. 21, lines 1-18).

Timmins relates to novel salts of metformin that are less soluble in water than known salts and can be formulated in a controlled release system that requires less polymer excipient to achieve a desired release rate (col. 2, line 26-43).

Sauerberg relates to compounds useful in the treatment of conditions mediated by nuclear receptors, in particular the Retinoid X Receptor (RXR) and the Peroxisome Proliferator-Activated Receptor (PPAR) families (Abstract). The formulations can be formulated for controlled release (col. 14, line 4-7).

C. Analysis

Independent claims 1 and 19, as amended, explicitly require a polymeric film that (i) reduces or prevents the interaction of the second drug and the first drug prior to administration of the dosage form; and (ii) dissolves in the gastrointestinal fluid upon ingestion.

M.P.E.P. § 2143.03, states "All words in a claim must be considered in judging the patentability of that claim against the prior art." [citations omitted]. In determining the differences between the prior art and the claims, the question under 35 U.S.C. §103 is not whether the differences themselves would have been obvious, but whether the claimed invention *as a whole* would have been obvious. M.P.E.P. § 2143.02.I.

Neither Johnson, nor Johnson in combination with Timmins and/or Sauerberg teach or suggest a dosage form having a polymeric film with the features as recited and claimed by Applicant.

Johnson teaches a dosage form that may be surrounded by a permeable membrane containing pores or holes (col. 3, lines 17-27; col. 5, lines 9-32 and 60-64; col. 7, line 49 – col. 11, line 5). In some embodiments, the membrane is made of an impermeable material and provided with holes or openings that may be drilled through the membrane (col. 7, line 49 – col. 8, line 8). These embodiments of Johnson are in stark contrast to Applicants' invention due to the holes or openings in the outer membrane. Specifically the dosage form of Johnson fails to reduce or prevent interaction of the drug in the core with a drug in an immediate release layer.

Moreover, Johnson fails to teach or suggest that the permeable membrane dissolves in the gastrointestinal fluid upon ingestion. Notably, none of the exemplified membrane materials recited in Johnson are capable of achieving this unique feature as claimed by Applicants.

Accordingly, the dosage forms Johnson fail to include a layer that prevents interaction of drugs in adjacent layers. Nor do the polymers employed by Johnson in the permeable membrane layer dissolve in the gastrointestinal fluid upon ingestion. These distinctions are significant, as one skilled in the art will recognize that the kinetics of drug release from a core surrounded by a dissolving film are very different from the kinetics of drug from a core surrounded by an insoluble membrane having pores or opening. Thus, the claimed dosage form is structurally different from the dosage form described by Johnson, and additionally results in a very different drug release profile.

In short, Johnson fails to teach or suggest the presently claimed method of manufacture and the dosage form as claimed by Applicants.

Secondary References

The cited secondary references, Timmins and Sauerberg, describe compounds that can be delivered using a controlled release system; however, these references fail to correct the defect in Johnson with respect to the recitation of a film/membrane that dissolves in the gastrointestinal fluid upon ingestion.

As none of the cited references, individually or in combination, teach or suggest a film or layer that (i) prevents the interaction of the second drug and the first drug prior to ingestion and (ii) dissolves in the gastrointestinal fluid upon ingestion, the cited references do not teach or suggest the claimed method or dosage form and therefore, fail to provide sufficient basis for a *prima facie* obviousness rejection. Withdrawal of the rejection is respectfully requested.

III. Double Patenting Rejection

Claims 1-28, 40, 41, and 43-46 were rejected on the ground of obvious-type double-patenting in view of claims 1-14 of Lim *et al.*, U.S. Patent No. 6,682,759 (herein "Lim").

A. The Present Claims

The present claims are set forth above.

B. Claims of the Cited Reference

The Lim patent includes two independent claims. The claims are to a method of manufacturing a pharmaceutical tablet. The claimed directed to a method includes two steps: (i) dispersing a second drug in a solid matrix to form a unitary core which upon immersion in gastric fluid releases the second drug by sustained release while retaining at least a portion of the mass of the solid matrix as a coherent body until said second drug is fully released therefrom, and (ii) depositing on the surface of the unitary core an aqueous suspension of particles of the first drug that are equal to or less than about 10 microns in diameter (claim 1) or (ii) combining particles of the first drug that are equal to or less than about 10 microns in diameter with particles of a second solid matrix to form an

immediate-release layer adjoined to the sustained-release layer as a layered tablet, the second solid matrix being of a substance that separates into discrete matrix particles immediately upon immersion in gastric fluid (claim 2).

C. Analysis

In determining whether a nonstautory basis exists for a double patenting rejection, the first question to be asked is: - does any claim in the application define an invention that is merely an obvious variation of an invention claimed in the patent? See, for example, M.P.E.P. at 804 II.B.1.

The claims of Lim relate to depositing on a first solid matrix (claim 1), or combining with a first solid matrix (claim 2), particles equal to or less than about 10 microns in diameter and having a second solid matrix to form an immediate-release layer. In contrast, the present independent claims (claims 1 and 19) require depositing on a unitary body (*i.e.*, solid matrix) a polymeric film that prevents the interaction of the second drug and the first drug prior to ingestion of the dosage form and that dissolves in the gastrointestinal fluid upon ingestion.

To arrive at the present claims starting with the claims of Lim, one skilled in the art would have to first add a dissolving film/layer between the solid matrix and the 10 micron particles, and then substitute an immediate release layer for the 10 micron particles, with the expectation that the dissolving film/layer would prevent the interaction of the second drug and the first drug prior to ingestion and dissolves in the gastrointestinal fluid upon ingestion.

The is nothing in the teaching of Lim, nor on the record, to suggest that one skilled in the art would modify the dosage forms defined by claims 1 and 2 of Lim in this manner, nor have any expectation that such a modification would yield dosage forms that work for the intended purpose of Lim. The present claims and those of Lim are not merely obvious variations of one another, but rather different inventions, at least because of the presence in the instant claims of a polymer film deposited between the solid matrix and the immediate release coating, and the presence of an a immediate release coating rather than a particulate layer. As such, the present claims are non-obvious and patentably

distinct when compared to those of Lim. Withdrawal of the rejection is respectfully requested.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the present claims are fully in condition for allowance. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4402.

Respectfully submitted,
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